High Lassa Fever activity in Northern part of Edo State, Nigeria: re-analysis of confirmatory test results

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SUMMARY

The purpose was to establish simple statistics of the effects of lassa fever in northern part of Edo State, Nigeria. Lassa fever activity in the northern part of Edo state, Nigeria, was confirmed in 2004 by laboratory analysis of samples sent to Bernhard–Nocht Institute (BNI) for Tropical Medicine Hamburg, Germany. The published report of that study is re-analysed to determine in statistical terms, what the values presented in percentages translate to in number of persons in the hospital and the area. In the year 2004, 12,000 persons presented with febrile illness at Irrua Specialist Teaching Hospital (ISTH), Irrua; 832 (6.5%) had lassa fever confirmed by reverse-transcriptase-polymerase chain reaction (RT-PCR). 4,096 (32.26%) of those with febrile illness had acute infection as they tested positive for IgM antibody. 333 (33.33%) of about 1000 staff of the hospital had sub-clinical infection as they tested positive for IgG and negative for IgM antibody. At least 208 of the 832 patients (25%) of the hospital with confirmed lassa fever must have died in the year 2004. 967 (5.9%) of relatives or members of the public who had contact with infected persons had confirmed lassa fever. 555 (66.67%) of those with confirmed lassa fever are close relatives. The epidemics occur in clusters of households, houses, streets or villages. It is concluded that high lassa fever activity in the area has wider effects than what is observed in hospital admitted patients. Further seroepidemiological survey involving large population sample in the area should be carried out to establish more accurate seroepidemiological data on lassa fever. This study is expected to impact positively on the generation of political priority for the control of lassa fever in Nigeria.

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Introduction

Lassa fever is an infection caused by lassa virus, a single stranded RNA virus. Lassa fever is a type of viral haemorrhagic fever with very high mortality rate in hospitalised patients. The disease is endemic in West Africa including Nigeria. The earliest record of the disease was in the 1950s but the virus was isolated by the Centre for Disease Control (CDC), Atlanta, USA, in 1969, from a sample taken from a missionary worker in Lassa village in northern Nigeria. A rat that is common in endemic areas, known as mastomys natalensis is the natural host of the disease.[1,2,3] Contacts with the rats including contamination of food by saliva, urine, excreta or other body fluid of the rat lead to the infection. Nosocomial transmission may occur through droplets by person-to-person contact or the contamination of needles. The symptoms and signs of the disease are similar and almost indistinguishable from other causes of fever in endemic areas such as malaria, typhoid, yellow fever, upper respiratory tract infection and other viral illnesses. The incubation period is 6 to 21 days. The symptoms and signs include fever, nausea and vomiting, chest pain, periorbital oedema, puffy face, puffy checks, oedema, dehydration, retrosternal pain, conjunctival injection, fainting attacks, bleeding from orifices, hypotension, shock and coma.[1-8] Other signs are pleural effusion,

ascites, cerebral oedema, adult respiratory distress syndrome and poor renal function [1-5] Simple diagnostic tests like bleeding time, whole blood clotting time and urinalysis may be helpful but non-specific. Thrombocytopaenia and lymphocytopaenia also occur in the disease. Other specific tests for accurate diagnosis are expensive and not generally available in the countries where the lassa fever is endemic. These tests include antibody IgG and IgM estimation, enzyme-linked immunosorbent assay (ELISA) for lassa virus antigen, reverse transcriptase polymerase chain reaction, immunofluorescence test and viral isolation. [1,2,3] The treatments include supportive measures like correction of hypotension, electrolyte and fluid replacement. Vaccines are expensive and not generally available or acceptable [4]. Surveillances include identification of close contacts for three weeks from the onset of the illness as well as the search for unreported and undiagnosed cases. Close contact of people in traditional burial ceremonies of infected corpses should be avoided. Overcrowding in hospitals especially in undiagnosed cases can lead to spread to other patients, staff and visitors in the hospitals. [1-8] Several cases of viral haemorrhagic fever from the northern part of Edo State, including Ekpoma, Uromi, Irrua, Igueben, Iruekpen, Igarra, Ibillo, Ozalla, Ubiaja, Agenebode, Auchi, Afuze, Akoko Edo, Ewu, Okpella and environs have been treated at the University of Benin Teaching Hospital, Benin City, from 1970 to 2000 with high fatality. There was no specific mention of lassa fever in all these years and no specific drug treatment or precautionary measure was available or adopted. With the establishment of Nigerian federal government-sponsored Irrua Specialist Teaching Hospital, Irrua, in the northern part of Edo State in 1992 (a teaching hospital for Ambrose Alli University, Ekpoma), several highly trained and motivated specialist doctors became available for teaching, research and treatment of diseases. The identification of large number of mastomys natalensis, the rat that is the natural host of the lassa fever virus led to attempts to identify the virus in patients with febrile illness in the area [5]. Careful history, clinical examination and assessment of sufferers with febrile illness that had periodic outbreaks led to the clinical diagnosis of lassa fever and requests for the equipment of the hospital or assessment of the samples from patients for specific diagnosis of lassa fever.[1,6,7,8] Clinical diagnosis was proven, remaining laboratory diagnosis including viral isolation. The federal government of Nigeria responded by erecting a lassa fever ward in the hospital and provided a project vehicle and ribavirin at no cost. Since then, patients with lassa fever have had some benefits of specific drug treatment. However, serological tests and viral isolation facilities were not available to define the magnitude of the problems in accurate statistical terms. This partly inhibited the development of political priority for the control of the infection since facts cannot be presented in simple statistical terms. In 2003, this problem was overcome with the help of a research team from BNI, Hamburg, Germany.

Materials and Method

In the years 2001, 2003 and 2004, large numbers of suspected outbreaks of lassa fever in the area led to a call from the hospital for special assistance. [6,7,8] To confirm lassa fever activity, samples were collected from ISTH between 2003 and 2004 involving patients suspected to have the disease, healthy contacts and some hospital staff. [8] These were sent to the Department of Virology, University of Lagos, Nigeria. After initial tests, the samples were later sent to Bernhard-Nocht Institute (BNI) for tropical medicine, Hamburg, Germany. BNI is a WHO collaborating centre for Arbovirus and Haemorrhagic fever reference and research. The result of the study was published [8] with isolation of the lassa virus including phylogenetic lineage and antibodies detection in healthy contacts and hospital workers. A total of 60 serum samples were collected and tested and the summary shows that 6.5 % of patient with febrile illness that were tested had confirmed lassa fever using reverse-transcriptase polymerase chain reaction (RT – PCR) and polymerase chain reaction (PCR). Serological tests for lassa virus-specific immunoglobulin G (IgG) and IgM were performed by indirect immunofluorescence assay by using cells infected with lassa virus strain Josiah. The virus was isolated in biosafety level 4 laboratories at BNI, Hamburg, Germany.

This study consists of re-analyses of the findings to find out what the figures from the results of this study amounted to in the number of persons in the hospital and the area concerning lassa fever activity.

Results

The report by the study at BNI is the proof of lassa fever activity in the area (Table 1). The magnitude of

Table 1. Lassa virus-specific findings in serum samples from Irrua SpecialistTeaching Hospital, Edo,Nigeria* (Table from Omilabu *et al*8)

Patient	RT-PCR	IgM titer	IgG titer
Patients with fever (n=31).			
04-10	Positive -	-	
04-02	Positive	1:40	-
04-51	-	1:160	-
04-34	-	1:40	-
04-03	-	1:,>20,480	1:20,480
04-05	-	1:320	1:20,480
04-01	-	1:160	1:10,240
04-08	-	1:80	1:20,480
04-33	-	1:20	1:640
04-52	-	1:160	1:40
04-53	-	1:40	1:40
Contact persons (n=17)			
04-04	positive	1:20	1:>20,480
03-04	-	1:160	1:80
04-11	-	-	
Hospital staff (n=12)			
04-31	-	-	1:80
04-32	-	-	1:80
04-17	-	-	1:80
04-20	-	-	1:20

*Data not shown for patients whose samples were negative in all tests.

the problems in facts and figures is shown in this result which is a re-analysis of the report. This study is to find out what the results of the 60 samples [8] translate to in normal daily life of the inhabitants of northern part of Edo State and Nigeria. This is shown as follows:

1. The number of patients seen at ISTH in 2004 was 16,000 and 80% of them had febrile illness [8] meaning that, 12,800 patients presented with febrile illness in the hospital in that year alone.
2. Two persons (6.5%) out of 31 persons with febrile illness that were tested had PCR-confirmed lassa fever [8] (Table 1). 12, 800 patients had febrile illness and (6.5%) of this means that 832 patients had confirmed lassa fever in that year from ISTH alone. This excluded those who visited other health institutions. If we assume 50% mortality since the number was not differentiated into children, elderly, pregnant women, adult and those not admitted in the hospital, this means that at least 384 persons died in that year from Lassa fever in Irrua Specialist Teaching Hospital alone.
3. Ten out of 31 patients (32.26%) with febrile illness had IgM antibody with or without IgG seropositivity for lassa fever virus [8] (Table 1). Therefore 32.26% of patients with febrile illness have positive IgM antibody. Presence of IgM antibody indicates acute infection. This translates to 4,096 persons that came to ISTH that year with febrile illness as having recent infection of lassa fever. This number excluded all patients who went to native doctors, herbal centres, other hospitals and clinics or who did not go anywhere or who may have died at home.
4. IgG in the absence of IgM was detected in 1 of the 17 contacts (5.9%) tested [8] (Table 1). This means previous exposure to the virus. 5.9% of tenants, co-tenants, close students, room mates, class mates and relations of patients with lassa fever were infected with the disease. In Africa, where polygamy, poor housing, overcrowding, high social support for sick persons and relations of death person are rampant, the real number will translate to hundreds of thousands of persons
5. IgG without IgM was detected in 4 of the 12 health care workers (33.33%) tested [8] (Table 1). Therefore since the number of hospital workers at ISTH is at least 1000, this translates to 333 of hospital workers having subclinical infection or having recovered from the disease 6. One of 17 asymptomatic contact persons (5.9%) had PCR-confirmed lassa fever at the time of sampling [8] (Table 1). This means that 5.9%

of contacts had confirmed lassa fever even though these persons were asymptomatic. In most African communities, at least 4 persons attend to a sick person, at least 4 persons sleep in a room or live closely in a house (the average student population in Ekpoma University in a room is 8 per room), we assume that 1 infected person would have had at least 4 contacts. Since from (3) above, 4,096 persons that came to ISTH had recent infection of lassa fever, we extrapolate that 4 contacts will amount to 16,384 members of the community. 5.9% of 16,384 will give 967 persons. Therefore 967 persons that are associated or had contacts with infected persons in ISTH in 2004 will have confirmed lassa fever.

7. Two (66.67%) of the 3 persons with confirmed PCR – positive for lassa fever were sisters living in the same house, had identical sequence of lassa fever showing closely related strains of lassa fever virus [8] Table 1. This also shows that 66.67% of lassa fever infection will occur in close relations possibly living in the same house. This is the trend observed in real life at ISTH as the epidemics occur in clusters of houses or villages.

8. Lassa fever circulating in the northern part of Edo State, Nigeria, (Nig 04 – 010) upon phylogenic analysis confirmed that it belongs to phylogenetic lineage II which is consistent with lassa virus strain circulating in the southern part of Nigeria with corresponding genetic and geographical origin.[8]

Discussion

Confirmation of lassa virus infection is a pre-requisite for ribavirin therapy. [1,2,3] Ribavirin is not always available in the hospital. Therefore health workers while saving lives do what appears as attempting suicide, since the mortality rate is high without drug treatment in confirmed cases and 33.33% of health care workers at ISTH were exposed to the disease [8]. There is no laboratory for specialised test for lassa fever in ISTH, patients are dying every day from the infection. This study shows that 832 patients had confirmed lassa fever in 2004 and this figure is 6.5% of patients with febrile illness [8] (Table 1). Much money was spent on Avian Flu in Nigeria yet only one confirmed mortality was recorded. Here, in northern Edo State, where lassa fever is ravaging youths, children and pregnant mothers and there is poor response in terms of drug supply or even advocacy.

Each year at least 32.26% (4, 096) of patients with febrile illness that come to ISTH have lassa fever. This figure may even be more than malaria and tuberculosis or HIV/AIDS. At least 5.9% of asymptomatic contacts had lassa fever confirmed and isolated from seven samples. [8] These figures should alarm all that are concerned that none is safe because if the asymptomatic contact travels to areas where lassa fever is not endemic such will not be treated for lassa fever since the drug is sent only to government hospitals in endemic areas of Nigeria.

Even though this study and the previous one [8] from which data was collected and extrapolated are limited in that they did not give mortality or fatality rate, or differentiate the infection into children, women, pregnant mothers or elderly, it has solidly confirmed the existence of an enormous problem.

We have undertaken this study as the authors agree with Shiffman [9,10,11,12] and other public policy researchers [13,14,15] that the existence of an indicator to mark the severity of the problem has a powerful effect of giving viability to that which has remained hidden and is therefore one of the strongest factors that determine whether an issue rises to the attention of policy makers. This study defined the clear message that the problem of lassa fever exists, it is killing inhabitants and visitors in the area and health care workers are at great risk. Contacts of infected persons including travellers and health and aid workers are at great risk and there is the need for adopting multiple criteria and capacity building in tackling the menace of lassa fever in West Africa.[13,14] A stitch in time, they say, saves nine. Attention is not paid to lassa fever in Edo State and in Nigeria as it deserves because there are not enough social entrepreneurs [15] and men of great calibre in Nigeria advocating for the prevention and treatment of the disease due mainly to its rural affectation and hence poor funding. [9,10,11,12] Since the deaths of leaders in Nigeria are not mostly from infection, there is tendency for leaders to ignore the great havoc of infectious diseases like lassa fever in Nigeria. [16] The breakdown of this result in simple statistical terms of its effect on the people is expected to generate the critically required international response which is so urgently needed in tackling lassa fever in West Africa and the world. [17] The fact that 5.9% of contacts got the infection places great risks on international travel and tourism worldwide. The fact that 832 patients are infected with the virus means that the government should as a matter of urgency improve the deplorable drug supply [18,19] pattern especially as it concerns ribavirin availability. The magnitude of

the problem also emphasises the need for community involvement in decision making process [20] regarding preventive measures, health education and health-seeking behaviours and vector eradication. Already a total of 24 confirmed lassa fever cases has been reported worldwide outside the West African sub-region and this number excluded non-reported cases and contacts of the reported cases.

In conclusion, there is high lassa fever activity in the area with high rate of infection of contact persons. These figures which were derived from re-analysis of confirmed cases of lassa fever infection are expected to impact positively on the political priority for the control of lassa fever in Nigeria. The statistics from this study are also expected to serve not only for monitoring purposes but also act as a catalyst for action to all the stakeholders involved in the control of lassa fever at both local and international levels.

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